Remarks

Support for the amendments to the claims

The amendment to claim 1 is supported by the specification as filed. *See* p. 2, lines 5 - 7, p. 4, lines 29 - 33, and p. 5, lines 9 - 14. The amendment to claim 9 is also supported by the specification as filed. *See* p. 2, lines 9 - 14, p. 4, lines 29 - 33, and p. 5, lines 9 - 14. The amendments to claims 2 and 16 merely correct typographical errors or add a comma between the preamble and the body of the claim. Thus, the amendments herein do not add new subject matter.

§ 102 Rejection

Claims 1 - 4 remain rejected under 35 U.S.C. § 102(e) as anticipated by LaPosta *et al.* The Examiner alleges that LaPosta *et al.* teaches all of the limitations of claims 1 – 4. The applicants respectfully traverse. LaPosta *et al.* does not anticipate because LaPosta *et al.* discloses a genus of compositions comprising a monophosphoryl lipid A composition. Among the components is a sugar, *see, e.g.*, col. 2, lines 3 – 5, which is selected from a group that includes trehalose. *See* col. 3, lines 24 - 27. Further *optional* components include antigens, *see* col. 2, lines 25-26, col. 2, lines 40-42, and col. 4, lines 8 – 9, one type of which that is mentioned is bacterial capsular polysaccharide linked to a protein carrier. *See* col. 4, lines 60 - 64. It is settled that a genus does not necessarily anticipate a species. *See In re Kollman*, 201 USPQ 193, 198 (CCPA 1979)(noting that the cited reference "fails to highlight the claimed composition among the many dozens disclosed"). Since LaPosta *et al.* does not specifically teach the combination of trehalose with a protein-polysaccharide conjugate, LaPosta *et al.* cannot anticipate claim 1 - 4.

Furthermore, the applicant notes that claim 1 has been amended to explicitly recite that the addition of trehalose to the polysaccharide-protein preserves immunogenicity. LaPosta *et al.* fails to teach this limitation.

This amendment to claim 1 does not narrow the scope of the claim because it merely recites explicitly a property of the claimed composition that was inherent in the unamended claim.

In addition, claim 1 has been amended to require that the vaccine composition be maintained in a liquid state. La Posta *et al.* does not teach this additional limitation. Thus, LaPosta *et al.* does not anticipate claims 1 – 4, as amended.

Not only does LaPosta *et al.* fail to anticipate the claims, it does not render them obvious, either. LaPosta *et al.* fails to teach or suggest that trehalose preserves the immunogenicity of the polysaccharide-protein over time. Nor does LaPosta *et al.* teach or suggest that trehalose is more effective than other sugars, such as lactose, at preserving the immunogenicity of the composition over time. Absent a teaching of this inherent property of the claimed composition, LaPosta *et al.* cannot render obvious claims 1 – 4.

§ 102/103 Rejection

Claims 9 - 10 remain rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over, La Posta *et al.* The Examiner considered and rejected applicants' argument that the stabilization of a liquid vaccine composition accomplished by the addition of trehalose is an unexpected result because the Examiner equated the effect of trehalose taught by LaPosta *et al.*, that is, prevention of aggregation, with stabilization. Furthermore, the Examiner takes the position that the applicants were arguing limitations that are not recited in the claims. The applicants respectfully disagree.

Although the Examiner is required to give claim terms the broadest reasonable interpretation, the Examiner's construction must still be enlightened by the written description. See M.P.E.P. § 2111. Nonetheless, claim 9 has been amended to recite the specific stabilizing effect caused by the addition of trehalose, that is, the preservation of immunogenicity. The amendment of claim 9 is merely meant to clarify the scope of the claim, and does not change the scope of the claim in any way. LaPosta *et al.* does not disclose, teach or reasonably provide any suggestion to combine trehalose with a polysaccharide-protein conjugate with any expectation that the immunogenicity of the polysaccharide would be preserved over time, as taught in the present application.

Claim 9 has been further amended to require that the vaccine composition be maintained in a liquid state. La Posta *et al.* does not teach this additional limitation. In light of the amendments to claim 9, the applicants respectfully submit that claim 9 is not obvious in light of LaPosta *et al.*

Furthermore, LaPosta *et al.* does not disclose, teach or reasonably suggest an amount of trehalose that is 3-12% by mass, as recited in claim 10. For this reason, and in light of the amendment to claim 9, the applicants respectfully submit that claim 10 is not obvious in light of LaPosta *et al.*

§ 103 Rejection

Claims 1 - 8 remain rejected under 35 U.S.C. § 103(a) as obvious over Anderson *et al.* and Roser *et al.* The applicants submit that Anderson *et al.* and Roser *et al.* do not disclose, teach or reasonably suggest all of the claim limitations in amended claim 1. To establish a *prima facie* case of obviousness, all of the claim limitations must be either taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981 (CCPA 1974), M.P.E.P § 2143.03. Neither Anderson *et al.* nor Roser *et al.* teach or suggest that a composition comprising trehalose and a protein-linked polysaccharide *preserves* the immunogenicity of the protein-linked polysaccharide over time. In fact, Roser *et al.* teaches that prevention of protein aggregates using trehalose is important as protein aggregates induce an "unwelcome" immune response. *See* p. 2, lines 15-25, p. 13, lines 16 - 20. Thus, Roser *et al.* teaches that it is desirable to *decrease* the immunogenicity of compositions containing proteins. Accordingly, the applicants respectfully submit that amended claim 1 (and dependent claims 2 - 8) cannot be obviousness in light of Anderson *et al.* and Roser *et al.*

Furthermore, the applicants submit that the Examiner has not properly considered all of the teachings of the cited references.

The Examiner states that "Anderson *et al.* teach that the conjugates of the invention appear to convert into macromolecular aggregates after preparation", citing to col. 13, line 67 – col. 14, line 2. However, this ignores the teaching in Anderson *et al.* as to the probable cause of the aggregation. Even though the conjugates in Anderson *et al.* were subject to lyophilization, Anderson *et al.* teaches that the aggregates formed "presumably by cross-linking from the formalin treatment." Col. 13, line 68 – col. 14, line 1. As acknowledged by the Examiner, nothing in Anderson *et al.* teaches or suggests the use of trehalose to prevent cross-linking of the immunogenic conjugates.

This deficiency is not cured by Roser *et al.* As indicated by the Examiner, Roser *et al.* indeed teaches the use of trehalose for the prevention of aggregation of a number of substances, but Roser *et al.* only teaches such a use for trehalose in a very narrow context: to prevent aggregation upon rehydration or thawing. *See* the Title and the Abstract. The Examiner's reference to the Title and the Abstract of Roser *et al.* for teaching the use of trehalose as a means of protecting substances from aggregation completely ignores the very narrow context of this teaching. Roser *et al.* does not disclose, teach or reasonably suggest the use of trehalose to prevent aggregation of substances

outside the dehydration/rehydration or freezing/thawing contexts. Without such a disclosure, it cannot be said that one of ordinary skill in the art would have been motivated to combine Anderson *et al.* and Roser *et al.* with a reasonable expectation of success to arrive at the claimed invention.

Furthermore, Anderson *et al.* and Roser *et al.* do not disclose, teach or reasonably suggest maintaining the vaccine composition in a liquid state, as recited by amended claim 1. As discussed above, Roser *et al.* only teaches the use of trehalose to prevent aggregation of substances in the dehydration/rehydration or freezing/thawing contexts, that is, when the substances are converted to solids. Nothing in Anderson *et al.* or Roser *et al.* suggests using trehalose in compositions maintained in the liquid state. Thus, the applicants respectfully submit that claims 1 - 8 cannot be obviousness in light of Anderson *et al.* and Roser *et al.*

Conclusion

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of the pending § 112, § 102, and § 103 rejections. If there are any questions or comments regarding this response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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